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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,006	12/21/2001	Nongnuch Inpanbutr	7331/US	8160

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EXAMINER	
BAHAR, MOJDEH	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 10/026,006	Applicant(s) INPANBUTR, NONGNUCH	
	Examiner Mojdeh Bahar	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's response to the office action of November 20, 2002 and the amendment, submitted March 18, 2003 is acknowledged. Applicant's amendment is persuasive to remove the objections in the previous office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-16, 18, 23 and 30-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Boggolini et al. (USPN 5,087,619).

Boggiolini et al. (USPN 5,087,619) teaches a composition comprising an effective amount of a vitamin D3 analogue (e.g., 1,25 $(OH)_2$ D3 and 1 alpha,25 dihydroxy- delta 16-23-yne-D3) employed in a method of treating neoplastic diseases in a warm-blooded animal, see for example tables III and IV, claim 20 and abstract. Boggiolini et al. (USPN 5,087,619) also teaches vitamin D3 analogues in oral dosage forms such as capsules, see col. 21, lines 37-40. Pharmaceutically acceptable carrier materials may be incorporated in capsules, such as starch, magnesium stearate, lactose, peppermint oil (flavoring agent), see in particular col. 21, line 37 to col. 22, line 27. Boggiolini et al. (USPN 5,087,619) also teaches that the dosage for the vitamin D3 analogues is 0.1 to 10 microgram per day, see col. 11, lines 16-24.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 13-23, 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boggolini et al. (USPN 5,087,619) and Yu et al (PMID 7756673).

Boggiolini et al. (USPN 5,087,619) teaches a composition comprising an effective amount of a vitamin D3 analogue (e.g., 1,25 $(OH)_2$ D3 and 1 alpha,25 dihydroxy- delta 16-23-yne-D3) employed in a method of treating neoplastic diseases in a warm-blooded animal, see for example tables III and IV, claim 20 and abstract. Boggiolini et al. (USPN 5,087,619) also teaches vitamin D3 analogues in oral dosage forms such as capsules, see col. 21, lines 37-40. Pharmaceutically acceptable carrier materials may be incorporated in capsules, such as starch, magnesium stearate, lactose, peppermint oil (flavoring agent), see in particular col. 21, line 37 to col. 22, line 27. Boggiolini et al. (USPN 5,087,619) also teaches that the dosage for the vitamin D3 analogues is 0.1 to 10 microgram per day, see col. 11, lines 16-24.

Yu et al. teaches that EB1089 is known to inhibit cell proliferation and is useful against neoplastic diseases, see abstract.

Boggolini et al. (USPN 5,087,619) and Yu et al (PMID 7756673) taken together do not teach the doses claimed herein in terms of nmol/Kg, neither do they teach all the pharmaceutical excipients and auxillaries claimed herein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ/express the amounts of active in terms of nmol/Kg. It would have also been obvious to employ any known pharmaceutical excipients and auxillaries in the composition employed in the instant method.

One of ordinary skill in the art would have been motivated to employ/express the amounts of active in terms of nmol/Kg because optimization of amounts is within the skill of the artisan and is therefore obvious. Similarly the employment of any known pharmaceutical excipient and/or auxillaries with a known active is within the skill of the artisan and therefore obvious. Note that by definition excipients are non-active ingredients of a composition. Absent a showing of criticality of a particular excipient or combinations of excipient it would be obvious to substitute one excipient for another or to employ a combination of excipients.

Claims 24-29, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boggolini et al. (USPN 5,087,619) and Yu et al (PMID 7756673) as applied to claims 13-23, 30-32 above, further in view of Katzung and Hardman et al.

Boggiolini et al. (USPN 5,087,619) and Yu et al (PMID 7756673) taken together do not teach the inclusion of a second active (i.e., bone agent, cytotoxic agent or anti inflammatory agent) in a composition employed in a method of treating cancer.

Katzung teaches that hypercalcemia is a consequence of hypervitaminosis D. Katzung further teaches that bisphosphonates, calcitonin are employed in treating hypercalcemia, see pages 661-663. Katzung also teaches the employment of estrogen inhibitors, mitomycin, vincristine, doxorubicin, fluorouracil for treating different cancers, see page 838 and 841. Katzung further teaches cisplatin, melphalan, and methoxorate as anti-cancer agents, see pages 830-832. Both Salicylates and Naproxen are known NSAIDS (known for their anti-inflammatory and analgesic properties), 537-538.

Hardman et al. teaches that pain is commonly associated with cancer, see page 539.

It would have been obvious to one of ordinary skill at the time the invention at the time the invention was made to employ a second active (i.e., bone agent, cytotoxic agent or anti inflammatory agent) in a composition employed in a method of treating cancer.

One of ordinary skill in the art would have been motivated to employ bisphosphonates and calcitonin in a method of treating cancer employing a vitamin D3 analogue/derivative because they are known to be employed in methods of preventing and/or treating hypercalcemia associated with vitamin D administration. One of ordinary skill in the art would have been motivated to employ Salicylates and Naproxen, known NSAIDS, known for their anti-inflammatory and analgesic properties, in a method of treating cancer because pain is known to be associated with cancer.

One of ordinary skill in the art would have been motivated to employ estrogen inhibitors, mitomycin, vincristine, doxorubicin, fluorouracil cisplatin, melphalan, and methoxorate along with Vitamin D derivatives in a method of treating cancer. Estrogen inhibitors, mitomycin, vincristine, doxorubicin, fluorouracil cisplatin, melphalan, and methoxorate are known to be

employed in methods of treating cancer. Combining two agents which are known to be useful to treat cancer individually into a single composition useful for the very same purpose (i.e. treating cancer) is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Response to Arguments

Applicant's arguments filed March 18, 2003 have been fully considered but they are not persuasive. Applicant first argues that the rejection under 35 USC 102 should be withdrawn since the reference, Baggiolini et al., does not teach a "food". In response to applicant's arguments, the recitation "food" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Even if the preamble were given weight, all claim limitations are still met. Note that the Webster's Collegiate Dictionary defines food as follows:

> "*any nutritious substance* that people or animals eat or drink or that plants absorb in order to maintain life and growth"
>
> "*material* consisting of essential body nutrients"

Therefore when food is given its broad dictionary definition, the cited prior art does indeed constitute food. Therefore a composition comprising Vitamin D does indeed meet the claim limitations and thus the rejection under 35 USC 102 is proper.

Applicant argues against the obviousness rejection in the prior office action stating that none of the references teach a food as claimed herein. For the reasons discussed herein above

this argument is nor persuasive. Applicant further argues that there is no motivation to combine the teachings of Baggiolini et al. with those of Yu. Note that as stated in the body of the rejection both these references teach the employment of vitamin D analogs herein in methods of treating neoplastic diseases. They thus teach the vitamin D analogs herein treat neoplastic disease in general and specific types of cancer in particular.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 from 8:30 a.m. to 6:30 p.m. Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
May 29, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER
6/1/03